医薬品　研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	総合機構処理欄
一般的名称	－		研究報告の公表状況	日刊薬業, 第 12105 号, 平成 18 年 9 月 6 日	公表国 日本	
販売名(企業名)	－					

研究報告の概要	使用上の注意記載状況・その他参考事項等
エイズウイルス(HIV)のうち、世界的にも感染例が少ない HIV-2 に日本人男性が初めて感染していたことがわかった。厚生労働省は、感染例の多い HIV-1 に比べ HIV-2 は感染力が弱いため、診断や治療などの体制は従来通りとする一方、HIV-2 の抗体検査の実施を徹底するよう都道府県に通知した。 HIV-2 は主に西アフリカで流行しており、感染してから発病までの期間が長いという。国内では 1993 年に韓国籍の 2 人の感染が確認されたが、今まで日本人の感染例は無かった。 男性は気管支喘息を患い、国内の医療機関に入院し、検査の結果、HIV-2 に感染していることが判明した。過去に西アフリカに渡航し、現地で輸血した経験があるため、これが感染経路と見られている。男性は既に症状が改善し退院している。 入院先の医療機関から依頼を受けた厚生労働省研究班が検査を行い、遺伝子検査の結果、HIV-2 であると確定、8 月 11 日に厚生労働省に報告した。 HIV 抗体検査で陽性だった場合には、抗体の種類を判別する確認検査を行うが、国内感染者のほとんどが HIV-1 のため、HIV-1 の検査だけをして HIV-2 の検査を行わない医療機関もあり得るため、厚生労働省では 8 月 11 日付で各都道府県に対し、HIV-2 の検査も確実に行い、検査漏れがないよう通知した。	「重要な基本的注意」に原材料となる血液について抗 HIV-2 抗体陰性を確認している旨を記載。

報告企業の意見	今後の対応
世界的にも感染例の少ない HIV-2 に感染した初の日本人男性に関する報告である。当社血漿分画製剤は原料血漿の段階で抗 HIV-2 抗体陰性を確認している。また、HIV に対するウイルスクリアランス指数が 9 以上であることを確認しているので、安全性について特に問題ないと考えられる。	今後とも HIV-2 に関する安全性情報等に留意していく。

厚労省　日本人初のＨＩＶ２型感染で検査徹底を通知

エイズウイルス（ＨＩＶ）のうち、世界的にも感染例が少ないＨＩＶ２型に日本人男性が初めて感染していたことが４日分かった。厚生労働省は、感染例の多いＨＩＶ１型に比べ２型は感染力が弱いため、診断や治療などの体制は従来通りとする一方、２型の抗体検査の実施を徹底するよう都道府県などに求めている。

２型は主に西アフリカで流行しており、１型に比べ感染力が弱く感染してから発病までの期間が長いという。国内では１９９３年12月と２００２年１月に韓国籍の２人の感染が確認されたが、今まで日本人の感染例はなかった。

男性は気管支喘息を患い、国内の医療機関に入院し、検査の結果、ＨＩＶ２型に感染していることが判明した。過去に西アフリカに渡航し、現地で輸血をした経験があるため、これが感染経路とみられている。男性はすでに症状が改善し退院している。

入院先の医療機関から依頼を受けた厚労省研究班が検査を行い、遺伝子検査の結果、２型であると確定、先月11日に厚労省に報告した。ＨＩＶ抗体検査で陽性だった場合には、抗体の種類を判別する確認検査を行うが、国内感染者のほとんどが１型のため、１型の検査だけをして２型の検査を行わない医療機関もあり得る。このため厚労省では先月11日付で各都道府県に対し、２型の検査も確実に行い、検査漏れがないよう通知した。

先端医療振興財団　助成事業の概要を公表

神戸市の先端医療振興財団は５日、２００７年度から実施する、「がん情報普及・啓発に関する講演会等への助成事業」の公募に関する概要を公表した。財団傘下の神戸臨床研究情報センター（神戸ＴＲＩ）の活動の一環で、１件当たり50万円、年間総額２５０万円を計上した。助成対象は、07年度に行われる市民・患者を対象にした、がん情報の普及啓発に関する講演会やシンポジウム。応募対象団体は日本がん患者団体協議会（ＪＣＰＣ）に加盟し、推薦を受けたＮＰＯ（民間非営利団体）などの民間団体。同一団体からの複数応募はできない。助成先は財団の審査委員会で決める。公募申し込み受付期間は９月15日～11月15日。詳細は、財団ホームページ（http://www.ibri-kobe.org/）で。

テムリック　第１種医薬品製造販売業許可を取得

ＣＲＯ（医薬品開発業務受託機関）のテムリックは４日、東京都から「第１種医薬品製造販売業」の業許可を８月24日付で取得したと発表した。ＣＲＯ業務とは別に行っていた、自社開発品の承認申請のために取得した。テムリックはがん領域に特化したＣＲＯとして２００２年に事業を開始したが、04年に「ＴＭ－４１１」（多発性骨髄腫）の開発権・販売権を導入し、創薬事業を始めた。同剤は現在治験実施中で、終了は来年以降になる見通し。今年４月にはすでに２品目としてシエーリングからがん治療薬の導入契約を締結し、７月末に「ＴＭ－５１１」として治験届を提出した。

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2006. 8. 22	該当なし	

一般的名称	洗浄人赤血球浮遊液	研究報告の公表状況		公表国
販売名(企業名)	洗浄赤血球「日赤」(日本赤十字社) 照射洗浄赤血球「日赤」(日本赤十字社)		H Cordel, I Quatresous, C Paquet, E Couturier. Eurosurveillance weekly release: 2006,volume 11, 8, 2006 Aug 10.	インド

研究報告の概要

○インドにおけるチクングンヤの再興:高まる脅威
チクングンヤウイルス(CHIKV)の感染がインドで拡大している。2005年12月以降最も被害の大きい5つの州から896,500人以上のチクングンヤ疑い症例が報告されている。北部の州からは1例も報告されていない。2004年末以降、チクングンヤはインド洋の南西部の島々で流行し、その後マダガスカルとインドでも報告された。インドにおけるチクングンヤは、1963年にコルカタで最初に検出された。1973年のインド西部での流行以降はサーベイランスは実施されておらず、インドから消滅したと考えられてきた。最近の研究では発症患者の約50%がRT-PCRでRNA陽性だったが、実際の発生率ははるかに高いと考えられる。病院に行かない患者が多く、受診してもRNA陽性となるのは1日目から4日目のみで臨床検査は難しい。症状は、38.5~40℃の高熱、筋肉痛、頭痛、関節の腫れと激痛、発症5日以降のかゆみを伴う斑点状丘疹で、多くは自己限定的で1~10日持続した。関節痛は症例の約10%で3週間以上持続し、数ヶ月~数年間続くこともある。温暖湿潤な気候と貯水池は媒介蚊の繁殖に適した環境で、貧しい人々はより感染しやすくなっている。インド洋のCHIKV分離株の遺伝子構造はウイルスが急速に変異することを示唆している。疾患は自己限定的であるが、流行地域への渡航者の感染リスクは引き続き存在する。輸入症例が欧州の多くの国から報告されており、フランスでは2006年3月に血液暴露によると考えられる国内感染例が発生している。媒介蚊の一つであるヒトスジシマカは欧州でも見られるため、ウイルス流入と地域内/持続感染のリスクについてさらに調査が必要である。
抗ウイルス剤とワクチンの開発が急務である。さらなる感染拡大を抑えるための対策の強化が求められる。臨床管理を改善する方法、特に早期検出、患者の栄養補給、その他の予防手段によって症状を大きく緩和できる。

報告企業の意見	今後の対応
チクングンヤウイルスの感染がインドで拡大しており、ヨーロッパへのウイルス流入と地域内感染が危惧されるとの報告である。	日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国後4週間は献血不適としている。今後も引き続き、新たなウイルス等による感染症の発生状況等に関する情報の収集に努める。

使用上の注意記載状況・その他参考事項等

洗浄赤血球「日赤」
照射洗浄赤血球「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

Resurgence of chikungunya virus in India: an emerging threat

SK Saxena[1] (shailen@ccmb.res.in), M Singh[1], N Mishra[1], V Lakshmi[2]

[1]Centre for Cellular and Molecular Biology, Hyderabad, India
[2]Department of Microbiology, Nizam's Institute of Medical Sciences, Hyderabad, India

Since December 2005, an outbreak of chikungunya virus (CHIKV) infection has been ongoing in various states of India (Karnataka, Maharashtra, Andhra Pradesh, Tamil Nadu, Madhya Pradesh, Gujarat, Orissa and Kerala) with potential spread to neighbouring states [1,2]. Cases were first recognised and reported in December 2005. In July 2006, India's National Vector Borne Disease Control Programme (NVBDCP) reported a reduction in the number of cases in the affected districts while other districts are now becoming affected for the first time. The spread is of unprecedented magnitude and over 896 500 suspected chikungunya cases have been reported since December 2005 from the five worst affected states (Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu and Madhya Pradesh) [3]. No chikungunya cases have been reported from the northern states.

Recent large-scale outbreaks of fever caused by CHIKV infection in India have confirmed the reemergence of chikungunya in this part of Indian subcontinent. Since the end of 2004, chikungunya has emerged in the islands of the southwestern Indian Ocean (Comoros, Mauritius, Seychelles and Reunion), where several hundred thousand cases have been reported. Chikungunya was later also reported in Madagascar and in India [4,5]. Chikungunya is not new to the Indian subcontinent. Since it was first detected in Calcutta in 1963 [6], there have been reports of CHIKV infection in different parts of India [7,8,9]. Previously, the most recent Indian chikungunya outbreak was reported in 1973 in western India, in Barsi, Sholapur district, Maharashtra state [10]. Subsequently, there has been no active or passive surveillance carried out in India and it was believed that chikungunya had disappeared from the Indian subcontinent [11,12].

A recent study looked at samples taken from over 140 symptomatic patients with clinical picture of chikungunya who were presented to the Nizam's Institute of Medical Sciences hospital in Hyderabad (the capital of Andhra Pradesh) in March and April 2006. About 50% were found positive for the presence of CHIKV specific RNA (through demonstration of the virus-specific 500 bp amplicon) by reverse transcription-polymerase chain reaction (RT-PCR) [V Lakshmi et al, unpublished data]. However, the true incidence is thought to be much higher, because due to the self-limiting nature of the illness a large proportion of patients did not go to hospital, and even for those who did, laboratory diagnosis proved difficult as RT-PCR was positive for the virus in samples collected between the first and fourth day only, indicating the viraemic phase of the infection. Most patients with acute CHIKV infection presented with high fever (ranging from 38.5°- 40°C), muscle pain, headache and swelling and severe pain in the joints with polyarthralgia (pain in several joints) followed by an itching maculopapular rash five days after onset. Symptoms were generally self-limiting and lasted 1-10 days. Almost 10% of cases reported had prolonged joint pain for more than three weeks. However, joint pain may persist for several months or years. Females were more affected than males, a feature probably associated with the daytime and indoor feeding habits of the mosquito vector in India, *Aedes aegyptii*. All age groups were evenly represented.

Warm, humid climates and water reservoirs serve as an excellent breeding ground for the vector of the virus, *Aedes* mosquitoes. With an increase in temperature, susceptibility of mosquitoes to CHIKV increases [13]. High population density, lack of adequate resources for vector control and hygiene added to the vulnerability of poor people to chikungunya infection. The unique molecular features of the recently analysed Indian Ocean isolates of CHIKV [4] suggest that the virus can evolve rapidly. Studies are in progress to confirm genomic structure and virulence of the recent CHIKV from India.

Although the disease is self-limiting, the risk to non-immune travellers from other parts of the world to areas with a chikungunya epidemic, including India, continues to exist and should be included in the differential diagnosis of travellers returning home with fever. The magnitude of this risk cannot be precisely determined at this time. There is a risk of importing the virus to Europe from affected parts of the world, including Africa and South East Asia, where the virus is endemic. Imported cases have been reported from a number of European countries, including an autochthonous case from France in March 2006, probably contaminated through a blood exposure incident [14]. Considering the extent of the current chikungunya outbreak, the risk of introduction and autochthonous/sustained transmission of the virus in Europe needs further investigation, because one vector, the tiger mosquito *A. albopictus*, is also present in Europe and could increase the likelihood of its future autochthonous transmission in these countries. Various recommendations have been suggested by European experts to ensure the measures to prevent the emergence of imported viral diseases are strengthened in

Europe [5,15]. Pregnant women, families with young children, older people, and those with significant comorbidity should be advised to consult their physician before travelling to the Indian subcontinent, and travellers should be informed about the magnitude of the risk of contracting the disease and decide according to their own judgment. There are no specific preventive medications or vaccines for chikungunya fever, but there are steps travellers can take to reduce risk of being bitten by infected mosquitoes [15]. Despite infecting millions of people worldwide, chikungunya infection has been neglected since its discovery. Worldwide, there are a number of other infections with mosquito-transmitted viruses (arboviruses) with similar symptoms which may be confused with chikungunya, such as Sindbis, Ross River and dengue, and these, together with a detailed travel history, should be considered in the differential diagnosis in returning travellers.

Considering high number of cases, and lack of specific antiviral therapy, it is imperative that specific antiviral agents and vaccine be developed. Although the disease is self-limiting, sustained and intensified control measures (such as regular fogging with pesticides, awareness of the disease and vector, detection and elimination of vector breeding sources, proper facilities for health care and community awareness about the prophylactic measures) are required to control the further spread of the disease. The government of India has taken up necessary steps, in accordance with the NVBDCP guidelines on reducing mosquito breeding sources, use of temephos larvicide in recommended doses, the release of larva-eating fish (*Gambusia*) into the wells and the water bodies to control the mosquito menace and deployment of mobile teams (three teams per district in the affected districts, consisting of epidemiologists, public health specialists, microbiologists and entomologists for assessment of the situation and providing technical assistance and guidelines) and mobilisation of health workers and volunteers [16,17]. Finally, measures to improve clinical management, especially early detection, nutritional support to the affected patients, and other preventive measures may largely mitigate the disease. The wider issues of ecology, current agricultural practices, water management systems, and human behaviour patterns will need to be reviewed. This requires a combination of strategies and we need to proceed with a sense of urgency in this matter.

References:

1. WHO Epidemic and Pandemic Alert and Response (EPR). Chikungunya and Dengue in the south west Indian Ocean. Disease Outbreak News, 17 March 2006. (http://www.who.int/csr/don/2006_03_17/en)
2. Four states affected by Chikungunya, says government. NewKerala.com website. 26 July 2006. (http://www.newkerala.com/news3.sphp?action=fullnews&id=28694) [accessed 01 August 2006]
3. Chikungunya - India (04). in: ProMED-mail [online]. Boston US: International Society for Infectious Diseases, archive no. 20060801.2120, 1 August 2006. (http://www.promedmail.org)
4. Schuffenecker I, Iteman I, Michault A, Murri S, Frangeul L, Vaney MC, et al. Genome microevolution of chikungunya viruses causing the Indian ocean outbreak. PLoS Med 2006; 3(7): e263. Epub 2006 May 23. (http://www.pubmedcentral.gov/articlerender.fcgi?tool=pubmed&pubmedid=16700631)
5. Depoortere E, Coulombier D. ECDC Chikungunya risk assessment group. Chikungunya risk assessment for Europe: recommendations for action. Euro Surveill 2006; 11(5): E060511.2. (http://www.eurosurveillance.org/ew/2006/060511.asp#2)
6. Shah KV, Gibbs CJ Jr, Banerjee G. Virological investigation of the epidemic of haemorrhagic fever in Calcutta: isolation of three strains of Chikungunya virus. Indian J Med Res 1964; 52: 676-83.
7. Jadhav M, Namboodripad M, Carman RH, Carey DE, Myers RM. Chikungunya disease in infants and children in Vellore: a report of clinical and haematological features of virologically proved cases. Indian J Med Res 1965; 53: 764-76.
8. Dandawate CN, Thiruvengadam KV, Kalyanasundaram V, Rajagopal J, Rao TR. Serological survey in Madras city with special reference to chikungunya. Indian J Med Res 1965; 53: 707-14.
9. Thiruvengadam KV, Kalyanasundaram V, Rajgopal J. Clinical and pathological studies on chikungunya fever in Madras city. Indian J Med Res 1965; 53: 729-44.
10. Padbidri VS, Gnaneswar TT. Epidemiological investigations of chikungunya epidemic at Barsi, Maharashtra state, India. J Hyg Epidemiol Microbiol Immunol 1979; 23(4): 445-51.
11. Pavri K. Disappearance of Chikungunya virus from India and South East Asia. Trans R Soc Trop Med Hyg 1986; 80: 491.
12. Ravi V. Re-emergence of Chikungunya virus in India. Indian J Med Microbiol 2006; 24: 83-4. (http://www.ijmm.org/article.asp?issn=02550857;year=2006;volume=24; issue=2;spage=83;epage=84;aulast=Ravi)
13. Mourya DT, Yadav P, Mishra AC. Effect of temperature stress on immature stages and susceptibility of Aedes aegypti mosquitoes to chikungunya virus. Am J Trop Med Hyg. 2004; 70(4): 346-50.
14. Cordel H, Quatresous I, Paquet C, Couturier E. Imported cases of chikungunya in metropolitan France, April 2005 - February 2006. Euro Surveill. 2006; 11(4): E060420.3. (http://www.eurosurveillance.org/ew/2006/060420.asp#3)
15. Chikungunya fever - information for travellers [Fact sheet]. European Centre for Disease Prevention and Control. 17 July 2006. (http://www.ecdc.eu.int/outbreaks/Chikungunya_reunion.php)
16. AP data shows Chikungunya declining. Sify Cities website. 27 June 2006. (http://sify.com/cities/hyderabad/fullstory.php?id=14236355) [accessed 22 July 2006]
17. Efforts on to control chikungunya. The Hindu. 14 July 2006. (www.hindu.com/2006/07/14/stories/2006071405140300.htm) [accessed 8 August 2006]

back to top

医薬品

医薬品　研究報告　調査報告書

化粧品

別紙 3-13

識別番号・報告回数		回	報告日 年　月　日	第一報入手日 2006 年 8 月 8 日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称			研究報告の公表状況	Simian foamy virus infection by whole-blood transfer in rhesus macaques: potential for transfusion transmission in humans Khan, A. S. and Kumar, D. Transfusion, 46, 1352-1359 (2006).	公表国 米国	
販売名（企業名）						

研究報告の概要	使用上の注意記載状況・その他参考事項等
アカゲザルでの輸血によるサル免疫不全ウイルス (SFV) の伝播が実験的に示されている。2 頭の自然感染したサルをドナー (D1 及び D2 と命名) として用い，各ドナーあたり 2 頭のレトロウイルス陰性サルに全血を輸血したところ，D1 から輸血された 2 頭のサルだけが感染した (追跡期間は輸血後 1 年間)。感染は以下の方法で証明された。 i) 輸血されたサルにおける特定 SFV 抗体の発現 ii) 感染ドナーサルの末梢血単核細胞 (PBMNCs) からの SFV 特有配列の PCR 増幅 iii) 末梢血単核細胞 (PBMNCs) からの感染及び複製 SFV の分離 興味深いことに，ドナーのサルはそれぞれ異なる複製動態を持つ SFV 菌株に感染していた (D1 の SFV は D2 の SFV よりも複製速度が早く，D2 は D1 より中和抗体価が顕著に高かった)。また，その他の要因，例えばウイルス接種量なども感染症の伝播において重要であると示唆された。	BYL-2006-0240 Detection and molecular characteri-zation of foamy viruses in Central African chimpanzees of the Pan troglo- dytes troglodytes and Pan troglodytes vellerosus subspecies. Calattini, S. et al, J. Med. Primatol. 35, 59-66 (2006).

報告企業の意見	今後の対応
これまで，非ヒト霊長類では SFV 感染による病変の報告は無かった。また，ヒトの感染例もほとんどなかった。しかし，SFVs は，in vitro で高い細胞変性を示し，ヌクレオチド配列は宿主ゲノム内で安定して取り込まれる。現時点では，ヒト間で SFV の伝播が起こるかは明らかではない。	現時点で新たな安全対策上の措置を講じる必要は無いと考える。引き続き関連情報の収集に努める。

Simian foamy virus infection by whole-blood transfer in rhesus macaques: potential for transfusion transmission in humans

Arifa S. Khan and Dhanya Kumar

BACKGROUND: Cross-species infection of humans with simian foamy virus (SFV) has been reported in European and North American nonhuman primate (NHP) handlers, primarily due to wound injuries involving infected animals in research centers and zoos. Additionally, African hunters have been found to be infected with SFV by exposure to body fluids, blood, or tissues of infected NHPs in the wild. The persistence of infectious virus in peripheral blood mononuclear cells (PBMNC) and the recent identification of some infected blood donors has raised safety concerns regarding potential virus transmission by blood transfusion.

STUDY DESIGN AND METHODS: SFV infection by blood transfusion was evaluated by whole-blood transfer from two naturally-infected rhesus macaques (designated as D1 and D2) to retrovirus-free monkeys. Blood from D1 was transfused to two recipient monkeys R1 and R2 and from D2 to monkeys R3 and R4. Virus transmission was evaluated by immunoassays, polymerase chain reaction assays, and coculture of PBMNC for SFV isolation.

RESULTS: SFV infection was seen in R1 and R2 based on development of virus-specific antibodies, identification of SFV sequences in monkey PBMNC, and isolation of infectious virus from PBMNC. Furthermore, both R1 and R2 remained SFV-positive at about 1 year after transfusion, which was the last time tested. No evidence of SFV infection was seen in R3 and R4.

CONCLUSION: SFV transmission in macaques occurred by transfusion of blood from one of two infected donor animals. These results indicate the potential of SFV transfusion transmission in humans, which may depend on virus-specific or donor-related factors.

Cross-species transmission of retroviruses to humans is an important public health concern as exemplified by the origin of human immunodeficiency virus (HIV) from simian immunodeficiency virus (SIV).[1] The extensive use of nonhuman primates (NHPs) in biomedical research and broad exposure to infected animals in the wild has facilitated cross-infection of humans with simian foamy virus (SFV), which is highly prevalent in all NHP species and possesses a broad host range and cell tropism.[2-4] The first human transmission was reported in 1971 due to injury by an infected chimpanzee.[5] Reports of cross-species human infection with SFV have increased since the mid-1990s[6-9] and the use of more sensitive detection assays have further indicated additional NHP handlers infected with SFV due to injury incurred by infected animals[10-12] as well as identification of people infected in Africa due to exposure to body fluids and meat while hunting and butchering of NHPs.[13]

It is noteworthy that although infectious virus has been demonstrated to persist long-term in human cells, in vivo and in vitro[6,14,15] there is, thus far, no report of disease associated with SFV and no evidence of SFV transmission between humans.[6]

The persistence of stably integrated, infectious retrovirus sequences in human peripheral blood cells raises

ABBREVIATIONS: CPE = cytopathic effect; IUPM = infectious units per million total PBMNC; NHP(s) = nonhuman primate(s); PBST = phosphate-buffered saline with 0.05 percent Tween; PBST+5 percent = PBST plus 5 percent milk; SFV = simian foamy virus; SIV = simian immunodeficiency virus; RT = reverse transcriptase.

From the Laboratory of Retrovirus Research, Division of Viral Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Bethesda, Maryland.

Address reprint requests to: Arifa S. Khan, PhD, 8800 Rockville Pike, HFM-454, Building 29B, Room 4NN10, Bethesda, MD 20892; e-mail: arifa.khan@fda.hhs.gov.

Received for publication March 14, 2005; revision received December 23, 2005, and accepted December 24, 2005.

doi: 10.1111/j.1537-2995.2006.00862.x

TRANSFUSION 2006;46:1352-1359.

concerns, however, regarding the safety of blood transfusion from SFV-infected blood donors. In fact, testing of archived sera identified six SFV-seropositive blood donors.[10] A retrospective study of four recipients of blood components (red cells [RBCs], filtered RBCs, and platelets [PLTs]) from one infected blood donor failed to demonstrate SFV infection; however, it was noted that additional studies are warranted to further evaluate the potential risk of SFV transmission by blood transfusion.[16] This is especially important since transmission by transfusion has been demonstrated as an important mode of acquisition of infections in humans with other retroviruses.[17,18] In this article, we have examined SFV transmission by whole-blood transfusion in a monkey model. Blood from SFV-infected donor animals was transfused into retrovirus-free monkeys, which were analyzed for SFV infection and persistence. This study evaluates the potential human risk of SFV infection by infected blood donors.

MATERIALS AND METHODS

Monkeys and blood transfusion

SFV-negative blood recipients were juvenile, rhesus macaques (*Macaca mulatta*) that were obtained from a group of animals in a domestic breeding colony (LABS of Virginia, Morgan Island, SC), which were free of SIV, simian T-lymphotropic virus, and simian retrovirus. Animals were identified as SFV-negative with a dot blot antibody assay[19] (Simian Diagnostic Laboratory, San Antonio, TX) and shipped in individual cages to the FDA animal facility (National Institutes of Health, Bethesda, MD). All animals were maintained in accordance with the *Guide for the Care and Use of Laboratory Animals* [20] under an approved protocol by the Institute Animal Care and Use Committee. The animals were housed in single cages and in a separate room from the SFV-infected blood donor monkeys. Only animals that were confirmed SFV-negative by serology and by polymerase chain reaction (PCR) analysis of peripheral blood mononuclear cell (PBMNC) DNA at the time of study initiation were used in the study. A control animal was housed in the same room as the blood recipient animals to demonstrate absence of cross-contamination due to housing and handling of the animals.

Donor animals, RhK3T and RhA2V (designated as D1 and D2, respectively, in this article) were adult rhesus macaques, naturally-infected with SFV that were maintained in single housing and in a separate room from SFV-negative animals. Donor animals were well characterized: SFV from D1 and D2 (designated as SFV-D1 and SFV-D2, respectively) were previously isolated from monkey PBMNCs and characterized in replication studies to evaluate virus fitness and nucleotide sequences were determined in the long terminal repeat region. The status of SFV infection in D1 and D2 was confirmed by serology and virus isolation from samples stored on day of blood transfer.

Blood was collected under sedation with ketamine hydrochloride (10 mg/kg). Before transfusion, blood was collected in anticoagulant (heparin or ethylenediaminetetraacetate [EDTA]) from the donor and recipient animals for preparation of PBMNC, plasma, and serum. At the time of transfusion, blood was collected in EDTA for additional PBMNC and plasma preparation and in separate tubes for blood chemistry and hematology. For blood transfer, blood (20 mL) was collected in heparin (1000 U, 1 mL, Elkins-Sinn Inc., Cherry Hill, NJ) from D1 for transfusion (10 mL each) with a butterfly catheter into the right saphenous vein of two recipient monkeys, RhCK2T and RhCK3H (designated as R1 and R2, respectively, in this article). Each animal was separately handled, and mats were changed in between each animal. Similarly, blood from D2 was transferred to RhCJ3K and RhCJ52 (designated as R3 and R4, respectively, in this article). After the blood transfer, 10 mL of saline was injected into a "housing control" animal RhOVG. Monkeys were monitored for healthy recovery after the blood transfusion based on temperature, heartbeat, and respiratory rate. After transfusion, blood was collected at various times in EDTA for PBMNC and plasma preparation for analysis of virus infection. Additionally, at each time of blood collection, serum chemistry and hematology were performed (Antech, Lake Success, NY).

Detection assays for SFV antibodies

SFV-specific antibody was detected by dot blot immunoassay[19] performed by the Simian Diagnostic Laboratory. The samples from each animal were collected and stored for concurrent analysis in the same assay.

SFV-seropositive animals were confirmed by Western blot analysis. Cell lysates were prepared from uninfected and SFV-2-infected *Mus dunni* cells (wild mouse fibroblasts; ATCC, Manassas, VA) as previously described.[21] Protein concentration was determined with a protein assay dye (Bio-Rad, Hercules, CA). Sixty micrograms of protein was heat-denatured and analyzed on an 8 percent Tris-glycine gel (Novex, San Diego, CA), run 1.5 hours at 125 V (Novex X-cell II system, Novex, San Diego, CA) in 1× Tris-glycine running buffer (24.8 mmol/L Tris, 192 mmol/L glycine, 0.1 percent sodium dodecyl sulfate). Proteins on the gel were transferred to nitrocellulose membrane (Invitrogen, Carlsbad, CA; 0.45 μm) at 30 V for 1 hour in 24.8 mmol per L Tris, 192 mmol per L glycine, 20 percent methanol. The membrane was cut into strips so that each strip contained 5 μg of protein. The strips were placed, protein side up, in individual wells of a plastic tray; rinsed at room temperature for 5 minutes each with Ultrapure water, phosphate-buffered saline (PBS) without Ca^{2+}-Mg^{2+}, PBS (pH 7.3)-0.05 percent Tween (designated as PBST); and blocked overnight at room temperature in PBST containing 5 percent nonfat dried milk (designated as